Amendments to the Specification

1. Please replace the paragraph beginning at page 12, line 14 with the following paragraph:

For purposes of comparing two different nucleic acid or polypeptide sequences, one sequence (test sequence) may be described to be a specific "percent identical to" another sequence (reference sequence) in the present disclosure. In this respect, when the length of the test sequence is less than 90% of the length of the reference sequence, the percentage identity is determined by the algorithm of Myers and Miller, *Bull. Math. Biol.*, 51:5-37 (1989) and Myers and Miller, *Comput. Appl. Biosci.*, 4(1):11-7 (1988). Specifically, the identity is determined by the ALIGN program, which is available at ~~http://www2.igh.cnrs.fr maintained by~~ IGH, Montpellier, FRANCE. A modified form of the ALIGN program may also be used. Typically the default parameters can be used. Preferably, a gap length penalty of 12 and a gap penalty of 4 can be used.

2. Please replace the paragraph beginning at page 12, line 24 with the following paragraph:

Where the length of the test sequence is at least 90% of the length of the reference sequence, the percentage identity is determined by the algorithm of Karlin and Altschul, *Proc. Natl. Acad. Sci. USA*, 90:5873-77 (1993), which is incorporated into the various BLAST programs. Specifically, the percentage identity is determined by the "BLAST 2 Sequences" tool, which is available at NCBI's website ~~http://www.ncbi.nlm.nih.gov/gorf/bl2.html~~. *See* Tatusova and Madden, *FEMS Microbiol. Lett.*, 174(2):247-50 (1999). For pairwise DNA-DNA comparison, the BLASTN 2.1.2 program is used with default parameters (Match: 1; Mismatch: -2; Open gap: 5 penalties; extension gap: 2 penalties; gap x_dropoff: 50; expect: 10; and word size: 11, with filter). For pairwise protein-protein sequence comparison, the BLASTP 2.1.2 program is employed using default parameters (Matrix: BLOSUM62; gap open: 11; gap extension: 1; x_dropoff: 15; expect: 10.0; and wordsize: 3, with filter).

3. Please replace the paragraph beginning at page 38, line 14 with the following paragraph:

Accordingly, the present invention provides protein complexes formed by interactions between Tsg101 and HIV GAGp6. The present invention also provides a protein complex having a homologue, derivative or fragment of Tsg101 interacting with HIV GAGp6. In

addition, the present invention further encompasses a protein complex having Tsg101 interacting with a homologue, derivative or fragment of HIV GAGp6. In yet another embodiment, a protein complex is provided having a homologue, derivative or fragment of Tsg101 and a homologue, derivative or fragment of HIV GAGp6. In another embodiment, the present invention encompasses a protein complex, or fusion protein, having a first polypeptide covalently linked to a second polypeptide, wherein said first polypeptide is Tsg101 or fragment or homologue or derivative thereof, and wherein said second polypeptide is HIV GAG or fragment or homologue or derivative thereof. In other words, one or more of the interacting protein members of a protein complex of the present invention may be a native protein or a homologue, derivative or fragment of a native protein.

4. Please replace the paragraph beginning at page 39, line 1 with the following paragraphs:

The protein complexes of the present invention contains a HIV GAG polypeptide as an interacting partner. In addition, GAG polypeptides and fragments thereof from other retroviruses containing the P(T/S/I)(A/T)P (SEQ ID NOs:1-6) late domain motif are believed to also interact with Tsg101 in the same manner as the HIV GAG polypeptide. Thus, they can be used in forming protein complexes with Tsg101 or a homologue or derivative or fragment thereof. Preferably, GAG polypeptides or fragments thereof of lentiviruses containing the P(T/S)AP late domain are used to form protein complexes. Such GAG polypeptides or fragments thereof may be from a non-primate lentiviruses including bovine lentiviruses (e.g. bovine immunodeficiency virus (BIV), Jembrana disease virus), feline lentiviruses (e.g. feline immunodeficiency virus (FIV) which causes immunodeficiency, wasting, and encephalitis in cats), and ovine/caprine lentivirus (e.g. caprine arthritis-encephalitis virus (CAEV) which causes anemia and wasting in goats, ovine lentivirus, Visna virus which causes pneumonia, wasting, encephalitis and arthritis). Preferably, the GAG polypeptides or fragments thereof are from primate lentiviruses including, but not limited to, human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), human immunodeficiency virus type 3 (HIV-3) (all of which cause AIDS), and various simian immunodeficiency viruses that infect hosts such as chimpanzee, mangabey, African Green monkey, mandrill, L'Hoest, Sykes' monkey, or Guereza Colobus monkey.

In one embodiment, the present invention encompasses an isolated protein complex comprising (a) a first protein that is (i) Tsg101 protein, (ii) a Tsg101 protein homologue having

an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6, (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, or (iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and (b) a second protein that is (1) HIV GAG polypeptide, (2) a HIV GAG polypeptide fragment, (3) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101, (4) HIV GAGp6 protein, (5) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101, (6) a HIV GAGp6 fragment capable of interacting with Tsg101, or (7) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide fragment, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAGp6 fragment.

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5. Please replace the paragraph beginning at page 53, line 24 with the following paragraphs:

4. Screening Assays

The present invention encompasses a method for selecting modulators of an interaction between a first protein and a second protein, wherein the first protein is (i) Tsg101, (ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6, (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, or (iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and wherein the second protein is (1) a retrovirus GAG polypeptide having the P(T/S)AP late domain motif, (2) a homologue of said retrovirus GAG polypeptide, said homologue having an amino acid sequence at least 90% identical to that of said retrovirus GAG polypeptide and capable of interacting with Tsg101, (3) a fragment of said retrovirus GAG polypeptide, said fragment being capable of interacting with Tsg101, or (4) a fusion protein containing said retrovirus Gag polypeptide, said retrovirus GAG polypeptide homologue or said retrovirus GAG polypeptide fragment. In a specific embodiment, the second protein is (1) HIV GAG polypeptide, (2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting

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with Tsg101, (3) HIV GAGp6 protein, (4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101, (5) a HIV GAGp6 fragment capable of interacting with Tsg101, and (6) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAgp6 fragment.

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The protein complexes of the present invention, Tsg101 and HIV GAGp6 can be used in screening assays to select modulators of Tsg101, HIV GAGp6, and protein complexes of the present invention. In addition, homologues, derivatives and fragments of Tsg101, HIV GAGp6, and protein complexes containing such homologues, derivatives and fragments may also be used in the screening assays. As used herein, the term "modulator" encompasses any compounds that can cause any forms of alteration of the properties, biological activities or functions of the proteins or protein complexes, including, e.g., enhancing or reducing their biological activities, increasing or decreasing their stability, altering their affinity or specificity to certain other biological molecules, etc. In addition, the term "modulator" as used herein also includes any compounds that simply bind Tsg101, HIV GAGp6, and/or the proteins complexes of the present invention. For example, a modulator can be a an interaction antagonist capable of interfering with, or disrupting or dissociating protein-protein interaction between Tsg101 or a homologue or derivative thereof and HIV GAGp6 or a homologue or derivative thereof.

6. Please replace the paragraph beginning at page 72, line 3 with the following paragraph:

Additionally, antibiotic resistance reporters can also be employed in a similar manner. In this respect, host cells sensitive to a particular antibiotics is used. Antibiotics resistance reporters include, for example, chloramphenicol acetyl transferase (CAT) gene and the kan^R gene, which confers resistance to G418 in eukaryotes and to kanamycin in prokaryotes. In one embodiment, the present invention encompasses a method for selecting modulators of an interaction between a first polypeptide and a second polypeptide, wherein the first polypeptide is (1) Tsg101 protein, (2) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6, or (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain; and the second protein is (1) HIV GAG polypeptide, (2) a

HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV Gag polypeptide and capable of interacting with Tsg101, (3) HIV GAGp6 protein, (4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101, and (5) a HIV GAGp6 fragment capable of interacting with Tsg101; wherein a host cell is provided having a first fusion protein having said first polypeptide, and a second fusion protein having said second polypeptide, wherein a DNA binding domain is fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second polypeptides; and providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first polypeptide and the second polypeptide.

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